REMARKS

Claims 49-95 are pending in the application, among which Claims 67.68 and 70-95 had been withdrawn from consideration. Of the latter, claims 70-82 are now cancelled without prejudice or disclaimer.

Claims 49-66 and 69 are active and were examined and rejected, while Claim 50 drew an objection.

Claim 49 has been amended for clarity, including recitation of "food storage containers" to provide an antecedent basis for later dependent claims (as discussed in the section concerning the §112, 2nd paragraph rejections.

Claims 51 and 61 has been amended voluntarily to improve clarity and to indicate that the phage "lyses contaminating bacteria" as an improved alternative to saying that the phage is "specific for bacterial contaminants"

The voluntary amendments in claims 57 and 62, together with the amendment of claim 49, cure the "antecedent basis" issue raised by the Action.

In claim 58, the members of the Markush group have been placed on separate lines and headed with a small Roman numeral, for greater clarity.

Claims 59-62 have been amended voluntarily to improve clarity and to indicate that the phage "lyses" *Listeria*, as an alternative to the language that the phage is "specific for" *Listeria*. Also, the claim now recites said lytic P100 phage" for greater clarify, although the inclusion of P100 here is not necessary in view of the claims' dependency. Claim 60 states that the phage is suspended in the liquid, as being more specific than "mixed with" the liquid. Also all instances of *Listeria* and *Listeria monocytogenes* have been italicized.

The composition claims have been amended to recite that the compositions comprise an isolated P100 phage, or an isolated A511 phage, as the case may be. Thus all the claimed compositions are based upon starting with isolated P100 phage as deposited (which constitute an isolated phage population) and recognized by ATCC Deposit Number PTA-4383. See also the paragraph bridging pages 11 and 12 regarding propagation and *purification* of phage.

Finally, as noted above, withdrawn claims 70-82 are cancelled whereas other withdrawn are retained, among which many are being amended voluntarily. These amendments are primarily intended to enhance clarity, in some cases using the same or similar language as in the amended composition and method claims under examination.

Claims 49-66 and 69 remain active for further examination. All of the amendments are supported in the specification and do not introduce new matter. Their entry and allowance is

respectfully requested. The claims are believed to define patentably subject matter and their allowance is earnestly solicited.

I. CLAIM OBJECTIONS AND RELATED COMMENTS

An objection to Claim 50 was raised because of what the Office correctly construed to be a typographical error where a disconnected "51" appeared at the end in line 2.

The claim has been amended to delete this extraneous "51".

Additionally, the Action pointed out that Claims 51, 61 and 65 each recite the biological name of a microorganism *(Listeria monocytogenes)* that should be italicized.

Applicants thank the Examiner for this "good catch" and have so amended each occurrence of biological names that are now written in italicized form.

II. REJECTIONS UNDER 35 USC § 112, FIRST PARAGRAPH (Enablement)

All pending claims (49-66 and 69) were rejected for lack of enablement, related to concerns about availability of the ATCC deposits.

The Action notes that since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. Alternatively, the requirements of 35 U.S.C. §112 may be satisfied by a deposit of the biological material. Because specification allegedly does not disclose a repeatable process to obtain the biological material, it is not apparent if the biological material is readily available to the public.

The Action reiterates that Applicants deposited the biological material (specification, at pages 2a and 3, in particular, or published application, US 2005/0175594 A1, paragraph [0006], in particular), but there is no indication in the specification as to public availability.

Applicant's Response **(Attorney Statement)**

The undersigned, as Applicants' Attorney, hereby states that the virulent/lytic phage P100 (ATCC Accession No. PTA-4383) and A511 (ATCC Accession No. PTA-4608), as recited in the instant claims, have been deposited under the conditions of the Budapest Treaty. The biological material will be irrevocably and without restriction or condition released to the public upon the issuance of a patent

In view of the foregoing statement, it would be proper to withdraw this ground for rejection.

III REJECTION UNDER U.S.C. § 112, 2ND PARAGRAPH

Claims 57 and 62 recite the limitation "said food storage container" or "said food storage containers", respectively. The Action notes a lack of antecedent basis for this limitation in the claims. The parent claim of both of these rejected claims recited the method step of "applying lytic phage P100…to a food product or food processing equipment," so that "said food storage container(s)" is deemed indefinite.

Applicants' Response

Claim 47 has been amended to recite clearly a "food storage container" which provides an antecedent basis for the noted language in claims 57and 62, which have been amended further as well. Applicants believe that the ground for rejection may now be withdrawn.

IV REJECTION UNDER U.S.C. § 101

Claims 63-66 and 69 were rejected as being directed to a non-statutory subject matter -- a product of nature, as they are directed to a composition comprising phage P100 (ATCC patent deposit designation number PTA-4383) and a carrier; said composition further comprising phage A511 (ATCC patent deposit designation number PTA-4608); the composition further comprising "an agent selected from the group consisting of listeriolysin, an enzyme, phage specific for bacterial contaminants other than *Listeria monocytogenes";* wherein said carrier is a pharmaceutically acceptable carrier; and Phage P100 (deposited at the American Type Culture Collection, ATCC patent deposit designation number PTA-4383).

The invention as claimed, allegedly reads on the natural products phage P100 alone and in combination with phage A511, or other phage) that are, according to the Office, substantially unaltered, and encompass (??) "compositions of food products (for example, cheese, dairy products, etc.) that are found contaminated with pathogenic bacteria such as *Listeria monocytogenes* (and/or other bacterial contaminants)." The invention, as recited, allegedly does not provide any structural distinction in the product as claimed, and the product resulting from bacterial contamination of food or . dairy products commonly occurring in nature. The Office has required explanation and/or correction.

Applicants Response

As Applicants understand the foregoing analysis, the Examiner believes that when *Listeria* organisms are found contaminating a food product, *etc.* in "nature", they are accompanied by a cohabiting population of P100 phages, or P100 + A511 phages, or a mixture of P100 phages and non-*Listeria* phages that lyse other bacteria whose presence on food products, *etc.,* is not desired.

Applicants respectfully disagree with this interpretation and, in support, respectfully direct the Examiner's attention to the Loessner Declaration, Sec. 9. The rejection is premised on the Office's assumption that the P100 phage composition claimed can be found in food products presumably unaltered by the hand of man. No scientific basis for this statement is provided. The way the Action reads, it appears that the "natural products" (understood to be the page in question)

> "encompass compositions of food products (for example, cheese, dairy products, etc.) that are found contaminated with pathogenic bacteria such as *Listeria monocytogenes* (and/or other bacterial contaminants).

Applicants are confused about the grammar of this sentence and, therefore, its meaning. What does it mean that "phages ....encompass compositions of food products."? Is the Examiner suggesting that the food products encompass (*i.e.*, contain, include, carry) the claimed phage particles? That is the meaning that Applicants have adopted and to which they respond here. The Action indicates that the "food products...are found contaminated with pathogenic bacteria such as *Listeria monocytogenes*." The meaning of that appears clear, and Applicants agree the fact that this happens. Indeed, that is why the present invention was made, to remove those natural contaminants of food. However, a connection appears to be missing.

(1) Is it the Office confusing bacteria with phages?

(2) Or is it the Office's position that because the bacteria are present, the phage must somehow be present as well?

If (1) is the intention, then the entire argument and basis for rejection is in error and the discussion can end here. If (2) is the intention, then Applicants, assisted by the Loessner Declaration, respectfully disagree.

First, if lytic P100 phage (or A511 phage) happened to be naturally present in the food product, the there would be no *Listeria* contamination because the phages would lyse their way through the bacterial population and eradicate it. This presents a logical conundrum. Moreover, as noted in the Loessner Declaration, the density of the *Listeria* population in a food product would not be sufficient to sustain the phage, which, if not infecting and growing on the bacteria (and lysing them) would disappear in short order. Thus, in Loessner's expert knowledge, and that in the art, it is simply wrong to assume or conclude that *Listeria* contaminated food harbors the P100 phage in its natural form as a natural contaminant. For these reasons alone, the §101 rejection should be withdrawn.

Even if any given phage such as P100 could be found naturally in food products, which Applicants re-emphasize it is not, it would be expected to be present in complex mixture with other *Listeria* phage, bacteria (both *Listeria* and other genera), phage specific for these other bacteria, *etc.*

Applicants have amended the composition claims, so that they are now directed to isolated P100 (or A511) phage. The claimed P100 phage have been acted upon by man in isolating (indeed discovering) and characterizing and propagating them to produce isolated and pure populations which have been deposited in the ATCC (as have the A511 phage). Any phages grown from these deposits (and separated away from the materials in bacterial lysates) would be such isolated P100 phage – not a product of nature for that additional reason.

So for the reasons advanced above, Applicants believe that the § 101 rejection should be withdrawn, particularly against the presently amended composition claims 63-66 and 69.

V. REJECTIONS UNDER 35 USC § 102(b) or§ 103(a)

Claims 63, 64, 66 and 69 were rejected as anticipated by or, in the alternative, as obvious over Loessner & Busse (1990) (hereinafter, "Loessner-I"); or Loessner et al (1996) (hereinafter "Loessner-II"). Claims 49-62, and 65 were considered to be free of this rejection.

As summarized in the Office Action, the claims are drawn to a bacteriophage P100 alone and in combination with another virulent phage A511, which lyses *Listeria monocytogenes* bacteria that contaminate various food, dairy products, and processing equipment.

The cited references allegedly disclose phage A511 This is said to be found

(a) in Loessner-I in the abstract, page 1914, Table 2, Results, *Bacteriophages,* in particular. and;

(b) Loessner-II at page 1133, right column and page 1134, left column, section on *Homologous recombination,* in particular),

The Action states that the disclosed A511 appears to be identical to the presently claimed strain since it produces same lysis or lytic phenotype on the bacterium, *Listeria monocytogenes.*

More surprisingly, however, the Action notes that the referenced microorganism (presumably, phage A511) disclosed in these documents

> "appears to be identical to the presently claimed phage P100 and is considered to anticipate the claimed microorganism since phage A511 is disclosed as being found to contaminate food, dairy products and processing equipments, and is of the same class or family *(i.e.* a myophage from the family myoviridae) as that of the microorganism claimed and is taught to be effective against the same bacterium, *Listeria monocytogenes).*"

Consequently, the Office goes on to conclude that P100 is anticipated by disclosure of phage A511, or its recombinant version as disclosed in these two references,

In the alternative, the Office Action contends that, even if claimed phage P100 is not identical to A511 in the references ***[which applicants assure the Office it is <u>not</u>; see below]***, as regard some unidentified characteristics "the differences between that which is

disclosed and that which is claimed are considered to be *so slight* that phage A511 is likely to possess the same characteristics of the claimed page P100 particularly in view of their shared characteristics with the *Listeria monocytogenes* host.

Under that reading, claimed phage P100 would have been obvious to those skilled in the art within the meaning of USC 103(a). So, the Office concludes that "the claimed invention as a whole was at least *prima facie* obvious, if not anticipated by the prior art references, especially in the absence of evidence (*i.e.,* a comparative data) to the contrary.

Applicants' Response

A. The Legal Test for Novelty:

"Anticipation requires the presence in a single prior art disclosure of all elements of a claimed invention arranged as in the claims". Jamesbury Corp v. Litton Industrial Products, Inc., 225 USPQ 253, 256 (Fed Cir 1985).

B. Legal Test for Nonobviousness:

The burden of establishing a case of *prima facie* obviousness rests with the Patent and Trademark Office. *In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Moreover, an obviousness rejection "must be based on *evidence* (statutory prior art, admissions against interest)..." *In re McKellin*, 188 USPQ 428, 432 (CCPA 1976), emphasis in original. The Federal Circuit has repeatedly articulated the requirements of a proper analysis:

> [W]here claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *See In re Dow Chemical Co.,* 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure.

In re Vaeck, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

It respectfully is submitted that the Office has not adduced a legally sufficient case of anticipation and has not met its burden required by the law in setting forth a *prima facie* rejection for obviousness over the Loessner-I and Loessner-II references for the reasons discussed below.

C. Applicants' Analysis of the Rejections

Applicants admit that they are somewhat puzzled with the fundamental legal and technical aspects of this rejection. The Office, relying on the concept that claims are to be interpreted as broadly a their terms reasonably allow, seems to have taken unusual liberties with

definitions and characterization of distinct types/strains of biological "organisms" (here, bacteriophages).

Because P100 and A511 are both lytic phage that lyse *L. monocytogenes* cells, they are being somehow equated (when the rejection is under § 102) or are considered to be interchangeable, obvious variants (when the rejection is under § 103), when there appears to be no basis in fact for such conclusions. This would be like saying that all lytic phages that lyse *E. coli* (which are much better known and have a glorious history in the evolution of microbial genetics/molecular biology) are the same, so if an objective was to lyse *E. coli* cells with a lytic coliphage, then knowledge that one phage class exists that lyses these bacteria would *per se* anticipate (or render obvious) any other lytic coliphage. Drawn even more narrowly, this analysis is like equating all the T-coliphages, or even the subset of the T-even or T-odd coliphages which are known to be different from one another, both within a subset and between subsets. Taken a step further, this logic is analogous to saying that *L. monocytogenes* bacteria are the same as, or obvious variants, of *Staphylococcus aureus* bacteria, because both are bacteria, both are gram-positive, both can be grown in culture, both can utilize glucose and other complex carbon sources, both encode this or that metabolic enzyme with analogous metabolic functions; both employ similar metabolic pathways, *e.g.*, glycolysis, both can form colonies on agar, both can be contaminants of ingested products, and both can make people sick. One could make the same arguments about *L. monocytogenes* and *E. coli*: both are bacteria, both can be grown in culture on not dissimilar nutrients, both have a bacillary appearance, both can colonize the human or other mammalian gut, both can make people or other animals sick (or not), *etc., etc.* Under such reasoning, a composition of, or method of using, *S. aureus*, or of *E. coli*, could be used to reject as anticipated a claim to an analogous composition or method involving *L. monocytogenes*, or would, *prima facie* render a such a *L. monocytogenes* composition or method obvious, merely based on the above sharing of selected properties. Applicants believe that the unreasonableness of this notion is clear on its face.

Applicants respectfully remind the Office that the inventors have developed, isolated, tested and can therefore make advantageous, practical use of a new type of phage that they discovered, isolated, propagated and characterized (and deposited in a public depository) that

(1) has a lytic host range that overlaps (but is not identical; see below) that of a different phage that was already known in the art,

(2) shares proteins in common, some with high sequence homology, but

(3) is nonetheless distinct.

Some of these distinctions are detailed in the Loessner Declaration. See, particularly Section 4. It should be borne in mind that the present inventors first discovered and disclosed the highly lytic, new, different, *Listeria*-specific phage, P100, independently of A511 and 6 and 12 years after publication of their cited papers describing A511. How is it possible that the existence of one biological "organism" can "suggest" another one that has not yet been discovered? How is it possible that the existence of one biological "organism" can or motivate a person skilled in the art (in the legal sense) to discover and develop a very particular, different organism even if it shares some properties, but is described as being advantageous for its intended uses?

Applicants do not deny that the A511 and P100 phages are "related" in terms of their genomic sequences, yet they are nevertheless distinct "chemical" or "structural" entities for which there is no basis to conclude that knowledge of the existence and properties of A511 anticipates a claim to P100 or renders such a claim obvious. This is not the same as comparing two small organic ring compounds that differ only in that the substituents in one are a methyl or ethyl group whereas the other is substituted at the same ring position with a propyl group.

Returning to the statements in Sec. 4 of the Loessner Declaration, P100 differs from A511 both in its host range as well as on the basis of its genome sequence and structure. This can be seen by examining the sequences in Genbank. The genomic sequence (131,384 bases) and the and encoded protein sequences of P100 is found in GenBank Accession #DQ004855 [1]. The same information on A511 (134,494 bases) is found in GenBank accession #DQ003638.[2]. Review of these sequences shows that P100 has 174 open reading frames and 18 tRNA-coding regions. A511 has 188 Open Reading Frames and 16 tRNA coding regions). Due to their length, copies of the database records are not included, and the Examiner can easily access them online.

In view of the foregoing remarks, Applicants believe that the Office has not met its burden under 35 U.S.C. §102(b) and 103(a), so the present rejection should be withdrawn.

VI. REJECTIONS UNDER 35 USC § 103(A) (Obviousness)

All the claims (49-66 and 69) were rejected as being obvious over Day *et al.* (US Pat. 5,006,347 (hereinafter "Day") in view of either one of Loessner-I or Loessner-II (*supra*).

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[1] See also: Carlton, R.M., Noordman, W.H., Biswas, B., de Meester, E.D. and Loessner, M.J.; "Bacteriophage P100 for control of *Listeria monocytogenes* in foods: Genome sequence, bioinformatic analyses, oral toxicity study, and application", *Regul. Toxicol. Pharmacol. 43*):301-312 (2005) (copy submitted herewith)

[2] Submitted directly by Dorscht, J., Zimmer. and Loessner, M.J., 11-APR-2005

Day allegedly discloses a method for retarding or controlling bacterial growth in cheese and use of bacteriophages for controlling unwanted bacterial contamination of food or fermentation of a food product such as cheese (citing to the Abstract, the claims, cols. 2- 4). The use of lytic phages is generally preferred as infection rapidly destroys the unwanted bacterial hosts such [*sic:* as] *Clostridium* and *Listeria* (col. 2, lines 38-41).

(Applicants note that this cited passage does not say "such [as] Clostridium and Listeria")

Day allegedly discloses that the phage containing composition can be in liquid or in lyophilized form (prepared by conventional techniques), and may be applied to a food product in an amount sufficient to cause reduction in bacterial growth (see column 3; 1st and 6th paragraphs, and claims,) in order to "reduce the amount of *Listeria.*"

(Applicants see nothing about "reduction in bacterial growth" and nothing about "Listeria" in the indicated para's of col. 3, nor anything explicit about "reduce the amount of Listeria" in the 1st and 6th "full" paragraphs of col. 3, or the claims)

Day allegedly disclose phage preparations or compositions that can comprise phages specific to several different bacterial species including *Listeria* (see column 2, lines 62-66, and claims).

Thus, it was concluded the reference teaches the use of phages specific for *Listeria* as well as composition suitable for controlling other food contaminating bacteria, such as *Clostridium*. The Office Action admits that there is no explicit teaching in Day of a method of controlling *Listeria* contamination in a food product, on food processing equipment, or on food storage containers comprising applying (a composition comprising) lytic phage P100 alone, or in combination with another lytic phage A511, though this is allegedly *"broadly suggested."*

(a point with which Applicants strongly disagree, as there is no such suggestion).

The Office's view of the teachings of Loessner-I and Loessner-II are discussed above, and Applicants remarks regarding these documents are relied upon in the same manner in this rejection. Briefly, the two cited Loessner references are cited as disclosing a composition comprising lytic phage A511 to aid in control (by lysis) of contaminating *Listeria monocytogenes* in or on a food product which ***{presumably 'the phage'}*** is **substantially identical** in the relevant characteristics such as virulent or lytic phenotype, to the claimed phage, and a host range that includes the commonly found bacterial contaminant, *Listeria monocytogenes.*

The Office concluded that, given the **detailed** disclosure in Day of the method for controlling *Listeria* contamination in or on food products such as cheese ***(also a characterization with which Applicants strongly disagree)*** (using compositions comprising bacteriophages against *Listeria* and/or other bacterial contaminants), the use of a bacteriophage composition comprising lytic phage A511,

(1) alone, as well as
(2) in combination with other type of lytic phage, or
(3) further comprising antibacterial agent such as a disinfectant, or an antibiotic

would have been obvious, "for the expected benefit of protecting the public against potential food contamination."

According to the Action, one of ordinary skill in the relevant art would have been motivated at the time of invention to modify in the Day process of using a phage composition by using, instead, an effective composition comprising bacteriophage A511, to control *Listeria* contamination in or on food products, as well as on food processing equipments, or on food storage containers, as explicitly suggested by the teachings of Loessner-I (citing to page 1912) and Loessner-II (for food safety, page 1133) for the expected benefit of protecting the public against potential food contamination with a **reasonable expectation** of success.

The claimed subject matter allegedly fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103(a). Thus, the invention as a whole would have been *prima facie* obvious to a person .of ordinary skill in the art at the time the claimed invention was made.

Applicants' Response

The legal test for obviousness was discussed briefly above. It respectfully is submitted that in making the above rejection, the Office again has not met its burden required by the law in setting forth a *prima facie* rejection for obviousness over Day in view of either the Loessner-I or Loessner-II references, for the reasons discussed below. Note that Applicants remarks above concerning obviousness over either of the Loessner references apply to the application of these references here too (as secondary references). The Loessner Declaration, and Applicants remarks based thereon, are set forth below and point to the weaknesses of the Day patent as an **enabling** disclosure as regards *Listeria* -specific phage (even when combined with either Loessner-I or Loessner-II, references) against the present claims all of which require, as a minimal feature, the P110 phage.

It is axiomatic and fundamental precept of U.S. patent law that to suffice as prior art, a disclosure must be enabling (*In re Donohue*, 226 USPQ 619,621 (Fed. Cir. 1985), in which the Federal Circuit stated that "even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling." Mere speculation alone about the preparation of a compound is never adequate to render that compound obvious. *In re Payne*, 606 F.2d 303, 203 USPQ 245 (CCPA 1979)

Judge Learned Hand declared in *Dewey & Almy Chem. Co. v. Mimex Co.*, 124 F.2d 986, 990, 52 USPQ 138 (@d Cir. 1942) that:

> No doctrine of the patent law is better established than that a prior patent must bear within its four corners adequate directions for the practice of the patent invalidated. If the earlier disclosure offers no more than a starting point for further experiments, if its teaching will sometimes succeed and sometimes fail, if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge and is not an anticipation.

These notions extend to references used in an obviousness rejection. Citing *Payne,* the court in *Beckman Instruments, Inc., v. LKB Producter AB* 892 F.2d 1547, 13 U.S.P.Q.2d 1301 (Fed. Cir. 1989) noted that in order to render a claimed apparatus or method **obvious**, the prior art must enable one skilled in the art to make and use the apparatus or method. See, also *White Consolidated Industries, Inc. v. Vega Servo-Control, Inc.*, 713 F.2d 788, 218 U.S.P.Q. 961 (Fed. Cir. 1983).

Indeed the above quote from 1942 represents a reasonable characterization of the present facts and the basis for the present rejection (as the cited prior art "offers no more than a starting point for further experiments," if even that).

The Prior Art Does not Teach nor Suggest the Present Invention

Applicants offer the following remarks, relying in part on the Loessner Declaration. At the time of the Day alleged "invention" the very *existence* of strictly lytic *Listeria* phage, *a fortiori*, the P100 phage of the present invention, was unknown. At the time the two cited Loessner papers were published, the P100 phage of the present invention was unknown. Therefore, there was no suggestion of this phage in either Day or the secondary references

As discussed in connection with the § 102 st rejection, above, phage P100 is a distinct entity from the A511 phage or any other phage.

Day's entire disclosure of the use of *Listeria* phage can be condensed to the following cites:

> "A suitable treatment may contain phages specific for two *Clostridium* **and** one *Listeria* species, for example." (at col. 2, line 64-66)

> Claim 4. " A method according to claim 1 wherein bacteriophage specificity is for bacteria selected from the group consisting of *Clostridia* spp. and *Listeria* spp."

This is clearly not an enabling disclosure for claims narrowly directed to any particular *Listeria* phage, namely, phage P100.

Even Day's disclosure of the use of *Clostridia* phages, the focus of most of the document, is believed to be defective as nonenabling, as discussed in the Loessner Declaration. Loessner states (Sec. 6), that no experimental proof exists for any of the assertions made in the Day patent with respect to the successful use of *Clostridia* phages in cheese or dairy products (or any contaminated food products). Based on his personal experience, Loessner stresses the difficulty of working with *Clostridia* phages and notes that his group was the first to publish a sequence of a *Clostridium* phage (about 15 years *after* Day's alleged "invention"). Also noted (Sec. 7) is the fact that, even today, no virulent phages are known or currently available for lysing the *Clostridium tyrobutyricum* bacterial species.

The Office's attention is respectfully directed to the following observations made by Loessner in the Declaration (Sec. 8):

(a) the life cycle of *Clostridium* species which exist as spores (not infectable by phage) and which must germinate in an anaerobic environment for bacterial growth and for susceptibility infection by phage and consequent lysis, and

(b) the general inapplicability of such anaerobic conditions in the food industry, particularly to the contamination of food products, [3] but even more so to food processing equipment, or food storage containers (see limitations of claim 1).

Given these facts, it is fair to conclude that Day falls short of enabling (scientifically) what is purportedly its own invention regarding *Clostridia* phages (to which most of the patent is devoted), *notwithstanding* the presumptions to the contrary for an issued U.S. patent. *A fortiori*, Day does not disclose in an enabling manner, nor does it suggest or motivate one skilled in the art to make/isolate and use any specific *Listeria* phage, let alone the P100 phage, for lysing *Listeria.* The secondary references do not overcome these deficiencies, as they suggest nothing about

(1) the new and distinct phage P100 as a composition or used in a method for treating food, food processing equipment or food containers to rid them of *Listeria* organisms, or

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[3] though one exception to this in the setting of food contamination might be in the center of large cheeses. The Loessner Declaration explains in Sec. 8 that in such a setting, any *Clostridia*-specific (or other) phages that were introduced into the product would be rendered useless.

(2) phage P100 in combination with A511 or any other phages that kill non-*Listeria* organisms at the same time.

Applicants contend further that the present obviousness rejection could be characterized as an application of an "obvious to try" standard which is known to be improper. This type of analysis was considered in detail by the Federal Circuit in *In re O'Farrell*, 7 USPQ 2d 1673 (Fed. Cir. 1988). The Federal Circuit expressly noted two common types of errors in basing an obviousness rejection on "obvious to try," one of which is more applicable here. This error presents itself when the claimed invention explores a new technology or new approach that seems to promising, "where the prior art gave only general guidance as to the partial form of the claimed invention or how to achieve it." *O'Farrell* at 1681.

In the present case, the Office's position that Day together with Loessner-I or Loessner-II provides one skilled in the art with a motivation or reasonable expectation of success in achieving the presently claimed compositions or methods. A careful reading of Day and consideration of the expert opinion in the Loessner Declaration (see above) shows that no such expectation is provided at all. The word "*Listeria*" appears only twice in the Day patent (see above). This is no more than a broad-brush disclosure, lacking any detail, regarding *Listeria* phage and their use in the context of food contamination. As noted above, there is **no** disclosure or guidance provided which can fairly be said to enable one of ordinary skill in the art to "make" or "use" **phage P100**. Whereas other phage that lyse *Listeria* were known and are disclosed in the secondary references, no teaching is provided there as to the existence, production or use of P100 phage – indeed this phage had not yet been conceived/discovered when those references were published. Knowledge and possession of this particular phage is a necessary condition for the compositions and methods of the presently claimed invention. Simply conjuring up a "desirability" factor derived from the Day (combined with one of the two Loessner references), could, at most, place the present invention in the category of "obvious to try." Said differently, even if, based on Day and the two Loessner references, it could be considered obvious (which Applicants contend it would not) to go forth and seek, find, characterize and isolate a new phage with advantageous properties for decontaminating food products of *Listeria* organisms, that would still not suggest or lead one to the present invention as claimed, based around P100. Nor would it provide a reasonable expectation that one would succeed in doing so. Thus, According to the law of obviousness, and the analysis of the *O'Farrell* court, this would not constitute a sufficient basis for an obviousness rejection.

As a final point, Applicants note that the Action referred repeatedly in its discussion of this rejection to "using the A511 phage". However, there is no claim directed to a method using the A511 phage, *per se*.. Rather, the method claims all include the P100 phage. Claim 50, which is the first to recite A511 phage, is directed to the use of P100 phage + A511 phage. Thus, the Office would be required to show that the use of P100, as well as the combination that includes P100, is obvious. As discussed above, the Office has not done so.

In view of the foregoing remarks and the Loessner Declaration, Applicants believe that this rejection under § 103(a) is improper and request that it be withdrawn.

VII. CONCLUSIONS

In view of the amendments to the claims and the foregoing remarks, Applicants believe that they have overcome or mooted the various grounds for rejection. Reconsideration, withdrawal of the rejections and allowance of the amended claims are respectfully requested.

The Examiner is invited to phone the undersigned at the number provided below if any further clarification is needed or to assist in any other way in the examination of this case.

Respectfully submitted,

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